

REMARKS

Entry of the foregoing and prompt and favorable consideration of the subject application is respectfully requested.

By the present amendment, the paper copy of the Sequence Listing for the subject application is added after the last page of the application to replace the sequence listing identified on pages 39-51. Pages 39-51 are deleted and the application pages are renumbered accordingly. A Request to Use the Computer Readable Form From Parent Application Pursuant to 37 C.F.R. § 1.821(e) and a Declaration Pursuant to 37 C.F.R. § 1.821 - .825 are being filed concurrently herewith.

A copy of the Abstract is submitted herewith on a separate piece of paper to be appended at the end of the disclosure.

Claims 3, 8, and 13-34 are canceled without prejudice or disclaimer of the subject matter disclosed therein.

Claims 1-2, 4-7, and 9-12 are amended to eliminate multiple dependency, to place them in better condition for U.S. patent practice, and to more clearly describe the claimed invention. Support for the amendments may be found throughout the application and in the claims as originally filed.

SECRET

APPENDIX

Marked up Claims

1. [Implant] An implant of genetically modified cells comprising an exogenous nucleotide sequence encoding all or part of an antibody directed against a tumor antigen or an epitope specific for an infectious and pathogenic microorganism, [the] said exogenous nucleotide sequence being place under the control of [the] elements necessary for its expression and for the secretion of [the said antibody.] said antibody, wherein said antibody is modified by fusion to a toxic or immunopotentiating substance, said antibody being functional and produced at levels of at least 50 ng/ml after reimplantation of said implant in an organism.

2. [Implant] The implant according to Claim 1, [characterized in that the] wherein said antibody is selected from the group consisting of:

- a native antibody,
- a chimeric antibody
- an antibody fragment, especially a fragment Fab, F(ab')₂, Fc, or scFv, and
- a bispecific antibody.

4 [Implant] The implant according to Claim [3, characterized in that the] 1, wherein said antibody [may be] is modified by fusion to a toxic substance selected from a ribonuclease, and especially the ribonuclease from *Bacillus amyloliquefaciens*, ricin, diphtheria toxin, cholera toxin, herpes simplex virus thymidine kinase, cytosine deaminase from *Escherichia coli* or from a yeast of the genus *Saccharomyces*, exotoxin from *Pseudomonas* and human angiogenin or an analog of [the] said substances.

5. [Implant] The implant according to [one of Claims 1 to 4, characterized in that] Claim 1, wherein the cells are genetically modified by transfection of a [vector derived from a plasmid, from a retrovirus or from a herpes virus, from an adenovirus,

from an] plasmidic, retroviral, herpetic, from an adenoviral, adenovirus-associated virus vector comprising [the] said exogenous nucleotide sequence placed under the control of the elements necessary for its expression and for the secretion of [the] said antibody.

6. [Implant] The implant according to Claim 5, [characterized in that the] wherein said vector is dicistronic.

7. [Implant] The implant according to Claim 6, [characterized in that the] wherein said vector is retroviral and comprises from 5' to 3':

- (a) a 5' retroviral LTR [derived from a retrovirus],
- (b) an encapsidation region,
- (c) an exogenous nucleotide sequence comprising:
 - an internal promoter,
 - a first sequence encoding the heavy chain of an antibody,
 - a ribosome entry initiation site,
 - a second sequence encoding the light chain of an antibody, and
- [(d) a 3' LTR derived from a retrovirus.]
 - a third sequence encoding a toxic or immunopotentiating substance fused downstream and operably to the second sequence; and,
- (d) a 3' retroviral LTR.

9. [Implant] The implant according to [one of Claims] Claim 1 [to 8], comprising genetically modified autologous cells.

10. [Implant] The implant according to Claim 9, comprising genetically modified fibroblasts.

11. [Implant] The implant according to [one of Claims 1 to 10, characterized in that it comprises] Claim 1, comprising from 10^6 to 10^{12} [, preferably from 10^7 to 10^{11}] genetically modified cells.

12. [Method] A method for the preparation of an implant according to [one of Claims 1 to 11, characterized in that] Claim 1, said method comprising contacting the genetically modified cells [and] with an extracellular matrix [are placed in contact].

12. [Method] A method for the preparation of an implant according to [one of Claims 1 to 11, characterized in that] Claim 1, said method comprising contacting the genetically modified cells [and] with an extracellular matrix [are placed in contact].